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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/720,410	12/21/2000	Joo Young Chung	G&C 118.US-W	9999

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GATES & COOPER LLP
HOWARD HUGHES CENTER
6701 CENTER DRIVE WEST, SUITE 1050
LOS ANGELES, CA 90045

EXAMINER

SPECTOR, LORRAINE

ART UNIT

PAPER NUMBER

1647

DATE MAILED: 11/20/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.



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This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

Responsive to communication(s) filed on 4/8/02

This action is FINAL.

Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

Claim(s) 1-12 is/are pending in the application.

Of the above, claim(s) 8, 10 is/are withdrawn from consideration.

Claim(s) is/are allowed.

Claim(s) 1-7, 9, 11, 12 is/are rejected.

Claim(s) is/are objected to.

Claim(s) 1-12 are subject to restriction or election requirement.

Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

Notice of Reference Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s). 4

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

Part III: Detailed Office Action

Election of Species Requirement:

Applicant's election with traverse of species Asn¹⁰⁸, Asn¹¹⁷, Asn¹⁶⁴ in Paper No. 9, filed 4/8/02, is acknowledged. The traversal is on the ground(s) that Applicants have identified specific glycosylation sites that give rise to hTPO derivatives that have biological activity equal to or greater than that of native hTPO, and that this is the unifying technical feature, not the generic concept of glycosylation of hTPO. This is not found persuasive because as stated in the species election requirement, neither hTPO nor glycosylation of such present an advance over the prior art. In particular, none of the individual mutations that contribute to the elected species are advances over the prior art, see art rejections below. Just as characterization of a prior art compound does not render that compound newly patentable, such characterization cannot form the basis of unity of invention as such is not a technical feature, but rather a property. Parenthetically, it is noted that applicants argue at page 4 of the response that there is "an increase in catalytic activity of the glycoprotein". It is noted that TPO is not known to be an enzyme, nor to have any catalytic activity.

The activity of TPO is the ability to bind to the mpl receptor and cause intracellular signaling by mpl.

The requirement is still deemed proper and is therefore made FINAL.

The claims are under consideration as they are drawn to the elected species, Asn¹⁰⁸, Asn¹¹⁷, Asn¹⁶⁴ hTPO, including all permutations of those three individual changes. Claims 8 and 10, limited to non-elected species, are withdrawn from consideration.

Formal Matters:

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed.

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The informal drawings are not of sufficient quality to permit examination with respect to

determination of the activity levels of the various disclosed muteins, which may be pertinent to patentability. Specific attention is directed to Figures 6, 7a and 7b, which use multiple symbols that are similar in shape and/or superimposed such that it cannot be determined which line corresponds to which species. In addition, there is no explanation of the term "normal" as it appears in the 5 figures; given the platelet levels identified as "normal", the Examiner suspects that "normal" represents an untreated control. Further, it is noted that Figures 7b and 8-12 are of insufficient copy quality for printing. Accordingly, new drawings are required in reply to this Office action.

Applicant is required to submit new drawings in compliance with 37 CFR 1.81 within the shortened statutory time period set forth for response to this Office Action. Extensions of time may 10 be obtained under the provisions of 37 CFR 1.136(a). Failure to timely submit new drawings will result in **ABANDONMENT** of the application.

Claims 1-7, 9, 11 and 12 are objected to because of the following informalities: The claims 15 encompass non-elected species, election having been made with traverse in paper number 4. The claims should be amended to be limited to the elected species. Appropriate correction is required.

Objections and Rejections under 35 U.S.C. §112:

20 The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Claims 6, 7, and 9 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The rejected claims require the availability of the vectors and cell lines recited therein. As a required element they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. The vectors and cell lines are described only by particular mutations therein, and not in so complete a manner that they could be predictably reproduced. Therefore, the specification does not provide a repeatable method for obtaining and it does not appear to be a readily available material. In such cases, the enablement requirements of 35 U.S.C. §112, first paragraph, may be satisfied by a deposit of the recited cell lines and vectors. See 37 C.F.R. §1.802. Accordingly, deposit of the recited vectors and strains is required for enablement in this case.

10 If a deposit is made under terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty *and* that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon 15 the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. §1.808.

16 If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or person associated with the patent owner (assignee) who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, should be submitted stating that the deposit has been made at an acceptable depository and that the 20 following criteria have been met:

(a) during the pendency of the application, access to the deposit will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent;

25 (c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 C.F.R. §1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 C.F.R. §1.809(d) should be added to the specification. See 37 C.F.R. §§ 1.803-1.809 for additional explanation of these requirements.

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Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

10 (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15 (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

20 Claims 1-5, 11 and 12 are rejected under 35 U.S.C. 102(e) as being anticipated by Elliott, U.S. Patent Number 5,756,083.

25 Elliott discloses and claims mpl ligand analogs having introduced N-glycosylation sites, including Asn¹⁶⁴, see claim 1, for example. The proteins were made using eukaryotic expression systems, see col. 14. At Table 7, columns 29-30, it is shown that some of the analogs had increased secretion from the host cells, and that the specific activity for most was comparable to unmodified human TPO. It is noted that the two most efficiently secreted forms had 3-4 and at least 5 N-linked chains.

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Claims 1, 3, 5 and 11 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Park et al., JBC 273:256-61, January 2 1998, cited by applicants. Park et al. disclose muteins of hTPO

L108N and R117N, disclosed as having 113% and 100.5% activity as compared to wild-type hTPO, see Table I, page 259. Eukaryotic expression vectors were used for the expression of such.

5 The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

10 (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

15 This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

20 Claim 12 is rejected under 35 U.S.C. 103(a) as being unpatentable over Park et al., JBC 273:256-61, January 2 1998, cited by applicants. The teachings of Park et al. are discussed above. Park et al. do not disclose a pharmaceutical composition. However, it would have been obvious to the person of ordinary skill in the art at the time the invention was made to make a pharmaceutical composition comprising the R117N mutein to be used for its known and disclosed properties of 25 inducing platelet production. Accordingly, the invention, taken as a whole, is *prima facie* obvious over the prior art.

Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elliott, U.S. Patent Number 5,756,083, in view of U.S. Patent Number 6,451,554 (Wood et al.).

30 The teachings of Elliott are summarized above. Elliott does not teach vector pcDNA3.1 or

the use of CHO K1 cells (which are dhfr) as host cells, which are the characteristic features of the vectors and cell lines of claims 6 and 7.

Wood et al. disclose that vector pcDNA3.1 is a preferred vector for recombinant expression, and is commercially available from Invitrogen; see column 7, lines 51-52. Wood et al. also disclose 5 CHO K1 cells as preferred host cells for recombinant expression; see column 9 at line 42. It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use vector pcDNA3.1 and CHO K1 host cells for production of the TPO muteins of Elliott et al. in view of the disclosure of Wood et al. that such were known and preferred in the art for such uses. Accordingly, in the express absence of any unexpected results, the claimed vectors and cells are 10 *prima facie* obvious over the cited prior art.

Claims 1-5, 11 and 12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Elliott in view of Park, and claims 6 and 9 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Elliott in view of Park and further in view of Wood et al.

15 This rejection is directed to the claims as they read upon the elected species, which is Asn¹⁰⁸, Asn¹¹⁷, Asn¹⁶⁴ hTPO.

The teachings of all three references are summarized above.

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to modify the hTPO Asn¹⁶⁴ mutein of Elliott et al. by adding the Asn¹⁰⁸ and Asn¹¹⁷ 20 mutations taught by Park et al. to make the claimed species. The person of ordinary skill in the art would have been motivated to do so by Elliott's teaching that the hTPO Asn¹⁶⁴ mutein was secreted more efficiently than native TPO and had comparable specific activity, combined with Elliott's teaching that the best secreted species had at least 3 glycosylation sites introduced, combined with Park's teaching that both the Asn¹⁰⁸ and Asn¹¹⁷ species retained at least wild-type activity. 25 Therefore, the person of ordinary skill in the art would have recognized that the 'triple mutein' would be expected to be secreted at least as well as, and have activity at least as high as that of native TPO. With respect to claims 6 and 9, the specifically claimed vectors and host cells are considered

prima facie obvious for reasons stated above with respect to claims 6 and 7. Accordingly, the claimed species is *prima facie* obvious over the prior art.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

Pearce et al., JBC 272:20595, 1997, disclose that an hTPO R117A mutein had greater activity than wild-type TPO, see page 20598, Table 1, and that residue 117 is in a solvent-exposed position on the TPO protein.

10 *Advisory Information:*

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Lorraine M. Spector, whose telephone number is (703) 308-1793. Dr. Spector can normally be reached Monday through Friday, 9:00 A.M. to 5:30 P.M.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Gary L. Kunz, at (703)308-4623.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

25 Certain papers related to this application may be submitted to Group 1800 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1 (CM1). The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Official papers filed by fax should be directed to (703) 872-9306 (before final rejection) or (703)872-9307 (after final). Faxed draft or informal communications with the examiner should be directed to (703) 746-5228.

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Lorraine Spector
Lorraine Spector, Ph.D.
Primary Examiner